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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,558	10/15/2003	Glen S. Kwon	33-02	7151

23713 7590 01/25/2007

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EXAMINER	
KISHORE, GOLLAMUDI S	
ART UNIT	PAPER NUMBER
1615	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/25/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary for Applications Under Accelerated Examination	Application No.	Applicant(s)	
	10/687,558	KWON, GLEN S.	
	Examiner	Art Unit	
	Gollamudi S. Kishore, Ph.D	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Since this application has been granted special status under the accelerated examination program,

NO extensions of time under 37 CFR 1.136(a) will be permitted and a SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE:

ONE MONTH OR THIRTY (30) DAYS, WHICHEVER IS LONGER,
FROM THE MAILING DATE OF THIS COMMUNICATION – if this is a non-final action or a *Quayle* action.
(Examiner: For **FINAL** actions, please use PTOL-326.)

The objective of the accelerated examination program is to complete the examination of an application within twelve months from the filing date of the application. Any reply must be filed electronically via EFS-Web so that the papers will be expeditiously processed and considered. If the reply is not filed electronically via EFS-Web, the final disposition of the application may occur later than twelve months from the filing of the application.

Status

1)☐ Responsive to communication(s) filed on _____.

2)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

3)☒ Claim(s) 1-14 is/are pending in the application.

3a) Of the above claim(s) _____ is/are withdrawn from consideration.

4)☐ Claim(s) _____ is/are allowed.

5)☒ Claim(s) 1-14 is/are rejected.

6)☐ Claim(s) _____ is/are objected to.

7)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

8)☐ The specification is objected to by the Examiner.

9)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

10)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

11)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

- See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 4-12-04; 8-4-04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims included in the prosecution are 1-14.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 4-5 and 12-15 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear whether the terms and expressions in parenthesis are indeed the limitations in claims 4 and 12.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

4. Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Onyuksel et al (6,217,886) of record.

Onyuksel et al disclose a method of preparation of micelles containing polyene compounds, Amphotericin B and Nystatin. The method involves dissolving the water insoluble compound and the lipid conjugated to a Water-soluble polymer (PEG-DSPE) in an organic solvent, removal of the organic solvent and hydrating the lipid film to form

micelles (col. 14, lines 15-47; claims 7-11 and 31). The composition further includes a cryopreservative (col. 14, line 67). What are lacking in Onyuksel et al are the pressure and temperature conditions under which the organic solvent is removed from the PEG-DSPE, active agent solution before hydrating it. However, in the absence of showing unexpected results, evaporation of a solvent is a manipulatable parameter in the highly developed chemical sciences. The examiner also points out that Onyuksel et al in Example 1 teach the use of rotoevaporator to remove the solvent. Since rotoevaporation is done under vacuum conditions, the pressure is lower than the atmospheric pressure even possibly including the claimed pressures. Onyuksel et al also lacks the teachings of the ratios of PEG-DSPE to amphotericin B. In the examples, Onyuksel et al teach the amounts of the active agent in terms of weight and not moles. In the absence of showing the criticality, it is deemed obvious to manipulate the basic teachings of Onyuksel et al to obtain micelles with the desired amounts of the active agents. Finally it should be pointed out that Onyuksel et al specifically disclose dextrose as the cryopreservative. However, since dextrose is a sugar and sugars are known cryopreservatives, one of ordinary skill in the art at the time the invention was made would expect reasonable expectation of success using dextrose.

5. Claims 1-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Moribe et al (Pharmaceutical Research 1998) of record.

Moribe et al disclose a method of preparation of liposomes containing polyene compound, Amphotericin B. The method involves dissolving the water insoluble compound and the lipid conjugated to a Water-soluble polymer (PEG-DSPE) in organic

solvents (methanol, chloroform), removal of the organic solvents and hydrating the lipid film to form liposomes (page 1738). What are lacking in Moribe et al are the pressure and temperature conditions under which the organic solvents are removed from the PEG-DSPE, active agent solution before hydrating it. However, in the absence of showing unexpected results, evaporation of solvents using different temperature and pressure conditions is deemed to be a manipulatable parameter in the highly developed chemical sciences. The amounts of amphotericin and PEG-DSPE reported by Moribe et al appear to fall within the broad ratios claimed in claim 8. Moribe et al also teach that the amount of amphotericin B encapsulated increased with the amount of PEG-DSPE used and with PEG molecular weight (abstract) and therefore, it is deemed obvious to one of ordinary skill in the art to vary the amounts of the PEG-DSPE and the molecular weight of PEG if higher amounts of encapsulated amphotericin is required.

6. Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Allen et al (US 2004/0013717) by itself or in view of Yu et al (Journal of Controlled Release, 1998) of record or vice versa.

Allen et al disclose micellar formulations containing PEG-DSPE to deliver any chemically or biologically active agent. The method of preparation involves dissolving the active agent and the phospholipid in an organic solvent, evaporation of the organic solvent using a rotary evaporator increasing the vacuum in increments of 25 mbar and hydrating the lipid film to form the micelles. The composition can be freeze-dried in the presence of a cryoprotectant such as a saccharide and rehydrated before use. The molecular weight of PEG is between 1000-10,000. (0016-0018, 0025, 0028, 0030,

0035, 0087, Examples 1 and 2). Although Allen et al do not specifically teach that the active agent to be amphotericin B, it would have been obvious to one of ordinary skill in the art to use any active agent including amphotericin B with a reasonable expectation of success since Allen et al teach its general applicability and provide guidance.

Yu et al teach polymeric micelles for the delivery of amphotericin. The polymer used for the formation of micelles is a PEG derivative of aspartic acid. According to Yu, the use of the polymeric micelles reduces the haemolytic activity of amphotericin B (abstract).

One of ordinary skill in the art would be motivated to use amphotericin B as an active agent in the micelles of Allen et al with a reasonable expectation of success since the reference of Yu et al shows the knowledge in the art of encapsulation of PEG containing polymeric micelles for the reduction of haemolytic activity of amphotericin B. Alternately, the use of PEG-DSPE instead of PEG-asp in the micelles of Yu et al would have been obvious to one of ordinary skill in the art since the reference of Allen et al shows that PEG-DSPE also forms micelles and such micelles could be used for the delivery of active agents. Although Allen et al do not specifically teach dextrose as the saccharide, the use of any saccharide would have been obvious to one of ordinary skill in the art with a reasonable expectation of success.

7. Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Onyuksel et al (6,217,886). OR Allen et al (US 2004/0013717) by itself or in view of Yu et al (Journal of Controlled Release, 1998) of record or vice versa as set forth above, further in view of McShane (6,906,042).

The teachings of Onyuksel et al, Allen et al, Yu et al have been discusses above. What is lacking in these references is the teaching of the use of dextrose.

McShane while disclosing micellar formulations teaches that lyophilized micellar preparations can be rehydrated with dextrose solution, which is suitable for intravenous administrations (col. 12, lines 15-23). The use of dextrose in the micellar compositions of Onyuksel et al, Allen et al and Yu et al would have been obvious to one of ordinary skill in the art since such a micellar preparation is suitable for intravenous administration as taught by McShane.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gollamudi S. Kishore, Ph.D whose telephone number is (571) 272-0598. The examiner can normally be reached on 6:30 AM- 4 PM, alternate Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Woodward Michael can be reached on (571) 272-8373. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gollamudi S Kishore, Ph.D
Primary Examiner
Art Unit 1615

GSK